UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,453	04/16/2001	Dan M. Granoff	CHIR-0283	1041

7590 12/28/2009

Alisa A Harbin
Chiron Corporation
Intellectual Property R338
PO Box 8097
Emeryville, CA 94662

EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
12/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/701,453	GRANOFF ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *091109*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-22 and 24-30* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☒ Claim(s) *26,27 and 30* is/are allowed.

6)☒ Claim(s) *17-19,21,22,24,25 and 28* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 09/11/2009 in response to the non-final Office Action mailed 04/20/09.

Status of Claims

2) Claims 24 and 28 have been amended via the amendment filed 09/11/09.

Claims 17-22 and 24-30 are pending.

Claims 17-22, 24-28 and 30 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Withdrawn

5) The objection to the specification made in paragraph 5 of the Office Action mailed 04/20/09 is withdrawn.

Objection to Specification

6) The specification is objected to for the following reasons:

37 CFR 1.75(d)(1) provides, in part, that 'the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description.' The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). The limitation 'a second carrier **comprising** polyglycolic acid**s** or polyglycolic acid**s** and the adjuvant' in the amended claim 24 [Emphasis added] and the limitation 'a second carrier comprising polyglycolic acid**s** or polyglycolic acid**s**' in the amended claim 28 lack clear support or antecedent basis in the specification.

Applicants contend that the specification on page 3, lines 8-15 indicates that carriers can be organic, inorganic, or both and further that the carrier can include (i.e., comprise) among other components 'polylactic acids, polyglycolic acids ....' and therefore, there is antecedent support for the second carrier as claimed. However, lines 8-15 of page 3 of the as-filed specification state the following:

> As used herein, the term "carrier" refers to a pharmaceutically acceptable component other than the NmB or NmC immunogenic component. The carrier can be organic, inorganic, or both. *Suitable carriers well known to those of skill in the art* and *include*, without limitation, large, slowly metabolized macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers, lipid aggregates (such as oil droplets or liposomes) and inactive virus particles. The carrier can also function as an immunostimulatory agent, e.g., adjuvant. Suitable adjuvants are well known to those of skill in the art.

This part of the specification supports suitable carriers well known to those of skill in the art, such carriers being polylactic acids or polyglycolic acids or an immunostimulatory adjuvant. The original claim 7 described aluminum hydroxide or MF59 as the second carrier, whereas the original claim 8 described a polylactic acid or a polyglycolic acid as the first carrier that is conjugated to NmC oligosaccharide. Likewise, the first and second full paragraphs on page 4 of the as-filed specification describe the first carrier being a polylactic acid or a polyglycolic acid, wherein the first carrier is conjugated to NmC oligosaccharide. A second carrier being alum or MF59 is supported at lines 16 and 17 of page 4 of the as-filed specification. However, these parts of the specification do not provide antecedent basis for 'a second carrier **comprising** polyglycolic acid**s** or polyglycolic acid**s** and the adjuvant' as recited in the amended claim 24 [Emphasis added] and for 'a second carrier comprising polyglycolic acid**s** or polyglycolic acid**s**' as recited in the amended claim 28. The statement in the specification that a carrier can also function as an immunostimulatory adjuvant does not support the MF59 adjuvant being comprised in a second carrier with polyglycolic acids or polylactic acids.

Rejection(s) Withdrawn

7) The rejection of claims 24 and 28 made in paragraph 10 of the Office Action mailed 04/20/09 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn in light of Applicants' amendment to the claims. A new rejection is set forth below to address the claims as amended.

Rejection(s) Maintained

8) The rejection of claims 17-19, 22 and 25 made in paragraph 12 of the Office Action mailed 04/20/09 under 35 U.S.C § 103(a) as being unpatentable over Granoff *et al*. (*Infect. Immun*. 65: 1710-1715, May 1997, of record) (Granoff *et al*., 1997) in view of Granoff *et al*. (*J. Pediatr*. 121: 187-194, 1992), Vella *et al*. (*Biotechnology* 20: 1-22, 1992, of record) and Frasch (*In*: *Development and Clinical Uses of Haemophilus B conjugate Vaccines*. (Ed) Willis *et al*. M. Dekker, New York, pages 435-453, 1994, of record), is maintained for the reasons set forth therein and herein below.

Applicants submit the following arguments:

(a) The Office has not established a *prima facie* case of obviousness. The Office has acknowledged that Granoff *et al.,* 1997 does teach the presence of outer membrane vesicles from serogroup B *Neisseria meningitidis* in their immunogenic vaccine composition. Therefore, Granoff *et al.* 1997 provides no information as to the interaction between MF59 and NmB OMVs. (b) Granoff *et al.* 1992 does not teach the presence of MF59 in their immunogenic vaccine compositions. Therefore, Granoff *et al.* 1992 also fails to provide any information regarding the interaction between MF59 and NmB OMVs. (c) MPEP § 2143 states that "combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable to one of ordinary skill in the art." One of skill in the art could not predictably combine Granoff *et al.* 1997 with Granoff *et al.* 1992 to produce the instant invention as neither provide any indication of how MF59 and NmB OMVs interact with one another. In order to establish a *prima facie* case of obviousness, the Office must provide at least a reason that one of skill in the art would combine the cited references. (d) Without knowing how MF59 and MenB OMVs interact, one of skill in the art would not necessarily expect to achieve the benefits of the PRP-OMP conjugate. The instant specification in Table 3 demonstrates that changing from alum to MF59 in the NmC conj. + NmB vaccines actually *decreases* the immune response to the NmB OMVs. At least in the context of the NMC conj. + NmB OMVs, MF59 appears to have a *deleterious effect* upon the NmB OMV's immunogenicity (though still sufficient for the inventors' purpose hereunder). Thus, one of skill in the art would not be motivated to combine PRP-OMP with NmC oligosaccharide and MF59, given the general unpredictability of combining different adjuvants. (e) The rational provided by the Office applies even to a lesser extent to claims 18 and 19 which require that the capsular oligosaccharide from serogroup *C N. meningitidis* (NmC) is conjugated to a protein

carrier. The Office has not demonstrated why one of skill in the art would not also conjugate NmC to OMV for the expected benefit of increasing immunogenicity. (f) Granoff *et al.* 1992 teach that the Hib-NmB conjugate results in a higher immune response after a single injection compared to the Hib-CRM197 conjugate and thus the apparent benefit is fewer injections with the Hib-NmB conjugate. However, if one of skill in the art were to combine NmC-CRM197 with the Hib-NmB conjugate, the combination would *most likely* not result in a sufficiently immunogenic response to the capsular oligosaccharide from serogroup *C N. meningitidis* (NmC) conjugated to the protein carrier after a single injection, because Fig. 1 of Granoff *et al.,* 1992 indicates that three injections were required for a CRM197 conjugate to give a strong immune response. There would be no reasonable expectation of success in combining NmC-CRM197 with Hib-OMV and MF59 to obtain the benefits of a strong immune response to both capsular polysaccharides after a single injection. Even if one of skill in the art were motivated to replace the Hib-CRM197 with Hib-OMV, one of skill in the art would *likely* also replace the NmC-CRM197 with NmC-OMV in order to obtain the presumed benefits of conjugating the capsular polysaccharides to the OMV. Claims 18 and 19 would not read upon such a modified vaccine composition where both the NmC and Hib are conjugated to OMVs and therefore would not be rendered obvious by the proposed combination of references.

Applicants' arguments have been carefully considered, but are not persuasive. The claims as presented currently do not require the recited MF59 to interact with the OMVs in a *specific manner*. As claimed, the MF59 is required to be present in the claimed composition along with the rest of the recited elements. The teachings of Granoff *et al*. (1997) as modified by Granoff *et al*. (1992), Vella *et al*. and Frasch taught the claimed composition as set forth previously. No where do the applied prior art references indicate that MF59 would eliminate the immunogenicity of the NmB OMVs. As acknowledged by Applicants, even with the MF59 present, the immunogenicity of the NmB OMVs was maintained at a sufficient level. Therefore, the argument of alleged lack of general predictability is not persuasive. Furthermore, the rejection of record did not set forth conjugating NmC to OMV for the expected benefit of increasing immunogenicity and therefore Applicants' argument on this issue is not relevant to the rejection of record. The Office Action did not state that claims 18 and 19 read upon a modified vaccine composition where both the NmC and Hib are conjugated to OMVs and therefore Applicants' argument on this issue is also not relevant to

the rejection of record. Granoff *et al.* (1997) indeed suggested the use of MF59 in combination with other vaccines. See first full paragraph in right column of page 1714. Granoff's (1997) conjugate composition containing MF59 did induce higher capsular antibodies even after the first dose. See last full paragraph on page 1711. Granoff's (1992) Hib-OMV conjugate also induced acceptably high levels of antibodies after three doses. See abstract; Figure 1 and Table II. Therefore, Applicants' argument on the alleged lack of reasonable expectation of success is not persuasive. Contrary to Applicants' assertion, sufficient reasoning has been set forth in paragraph 12 of the Office Action mailed 04/20/09 to establish a *prima facie* case of obviousness. The rejection stands.

9) The rejection of claim 21 made in paragraph 13 of the Office Action mailed 04/20/09 under 35 U.S.C § 103(a) as being unpatentable over Granoff *et al*. (*Infect. Immun*. 65: 1710-1715, May 1997, of record) (Granoff *et al*., 1997) as modified by Granoff *et al*. (*J. Pediatr*. 121: 187-194, 1992), Vella *et al*. (*Biotechnology* 20: 1-22, 1992) and Frasch (*In*: *Development and Clinical Uses of Haemophilus B conjugate Vaccines*. (Ed) Willis *et al*. M. Dekker, New York, pages 435-453, 1994) as applied to claim 17 above, and further in view of Dalseg *et al.* (*In*: *Vaccines* 96. (Ed) Brown F. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., pages 177-182, 1996, of record), is maintained for the reasons set forth therein and herein below.

Applicants contend that the Office has not established a *prima facie* case of obviousness as there is no reasonable expectation of success for the particular combination of Granoff *et al.,* 1997 and Granoff *et al.,* 1992. The Office has not demonstrated how Dalseg *et al.* could provide a reasonable expectation of success where the other art cited has not.

Applicants' arguments have been carefully considered, but are not persuasive. As set forth *supra*, the Office has established a *prima facie* case of obviousness with regard to the teachings of Granoff *et al*. (1997) as modified by Granoff *et al*. (1992), Vella *et al*. and Frasch. In paragraph 13 of the Office Action mailed 04/20/09, the Office has clearly set forth therein how Dalseg's teachings are relevant to the rejection of record. The rejection stands.

10) The rejection of claim 24 made in paragraph 14 of the Office Action mailed 04/20/09 under 35 U.S.C § 103(a) as being unpatentable over Granoff *et al*. (*Infect. Immun*. 65: 1710-1715, May 1997, of record) (Granoff *et al*., 1997) as modified by Granoff *et al*. (*J. Pediatr*. 121: 187-194, 1992), Vella *et al*. (*Biotechnology* 20: 1-22, 1992) Frasch (*In*: *Development and Clinical Uses of Haemophilus B conjugate Vaccines*. (Ed) Willis *et al*. M. Dekker, New York, pages 435-453, 1994)

as applied to claim 17 above, and further in view of Seid (US 6,638,513, of record) ('513) or Granoff (WO 98/58670) ('670), is maintained for the reasons set forth therein and herein below.

Applicants contend that the Office has not established a *prima facie* case of obviousness as there is no reasonable expectation of success for the particular combination of Granoff *et al.,* 1997 and Granoff *et al.,* 1992. The Office has not demonstrated how Seid ('513) or Granoff ('670) could provide a reasonable expectation of success where the other art cited has not.

Applicants' arguments have been carefully considered, but are not persuasive. As set forth *supra*, the Office has established a *prima facie* case of obviousness with regard to the teachings of Granoff *et al*. (1997) as modified by Granoff *et al*. (1992), Vella *et al*. and Frasch. In paragraph 14 of the Office Action mailed 04/20/09, the Office has clearly set forth therein how Seid's ('513) or Granoff's ('670) teachings are relevant to the rejection of record. The rejection stands.

New Rejection(s) Necessitated by Applicants' Amendment

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

11) The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12) Claims 24 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The dependent claim 24, as amended now, includes the limitation: wherein said composition comprises 'a second carrier **comprising** polyglycolic acids or polyglycolic acid**s** and the adjuvant' [Emphasis added]. Claim 24 depends from claim 17, which recites that the adjuvant is MF59. The dependent claim 28, as amended now, includes the limitation: said composition 'further comprises a second carrier **comprising** polyglycolic acids or polyglycolic acid**s**'. Claim 28 depends from claim 26, which is drawn to an immunogenic composition which does *not* comprise *a first carrier*. Thus, 'a second carrier' recited in the amended claims 24 and 28 is a generic carrier that comprises within it polyglycolic acids or polyglycolic acids and the MF59 adjuvant and a generic carrier that comprises within it polyglycolic acids or polyglycolic acids respectively. Applicants mention of the Office's alleged

acknowledgement that claims 24 and 28 contemplate the polylactic acids or polyglycolic acids as 'within a generic carrier, which encompasses organic carrier, inorganic carrier, cellular carrier, bacterial carrier, etc.' Applicants assert that the specification on page 3, lines 8-15, indicates that carriers can be organic, inorganic, or both and further that the carrier can include (i.e., comprise) among other components 'polylactic acids, polyglycolic acids ....' and that the carrier can also function as, and therefore include, an immunostimulatory agent which can include an adjuvant such as MF59. Applicants state that they have clarified claims 24 and 28 so that it is clear that there is a second carrier that comprises MF59 and the polylactic acids or polyglycolic acids. However, as explained *supra* under paragraph 6, the above-identified limitations in the amended claims and the current scope of the claims lack support in the specification as filed. Contrary to Applicants' assertion, the Office did not acknowledge that claims 24 and 28 'contemplate' the polyglycolic acids or polyglycolic acids within a generic carrier. Instead, the Office rejected claims 24 and 28 for new matter under 35 U.S.C 112, first paragraph for the newly added limitation 'a carrier **comprising** polyglycolic acid**s** or polyglycolic acid**s**' [Emphasis added]. The addition of new unsupported limitations to claims years after the filing of the application does not constitute contemplation, but constitutes new matter. Therefore, the above-identified limitations in the claim(s) are considered to be new matter. New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed by pointing to specific lines and pages, for the new limitations, or alternatively, remove the new matter from the claim(s). Applicants should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

13) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

14) Claim 28 is rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 28, as amended, is indefinite and confusing in the limitation: 'further comprises a *second* carrier' [Emphasis added]. Claim 28 depends from claim 26, which does not recite a first carrier or any carrier. It is unclear how 'a carrier' recited in the claim becomes 'a second carrier'.

Relevant Art

15) The relevant art made of record and not currently relied upon in any of the rejections is considered pertinent to Applicants' disclosure.

- The art recognizes the desirability to include in a vaccine 'any number of different substances referred to as adjuvants …. to stimulate the appropriate portion of the immune system'. See paragraph bridging columns 12 and 13 of Stapleton *et al*. (US 5,846,735) and paragraph bridging columns 13 and 14 of Hofmann *et al*. (US 6,193,971).

Remarks

16) Claims 17-19, 21, 22, 24, 25 and 28 stand rejected.

Claim 20 is objected to as being dependent from a rejected claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 26, 27 and 30 are allowable.

17) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no

event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

19) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

20) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

December, 2009